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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 10/812,551
Filing Date: March 29, 2004
Appellant(s): BUCOLO ET AL.

Joseph Barrera
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal briefs filed 04/15/09, 05/19/09, and 06/08/09 appealing from the Office action mailed 04/01/09.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief dated 04/15/09 is correct.

(8) Evidence Relied Upon

Singh et al (US Pregrant Pub 2003/0232089)

Olejnik et al (US 5,597,599)

Gohzu et al (US 5,013,445)

Cantoro et al (US 5,770,628)

Katz (US 4,287,175)

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

Claims 1, 6-11, 25-28, and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al (US Pregrant Pub 2003/0232089, see IDS dated 06/24/2004) in view of Olejnik et al (US 5,597,599) and Gohzu et al (US 5,013,445).

Singh et al teaches trishydroxymethylaminomethane as a buffering component (paragraph 93) for ophthalmic gum compositions (abstract) where the composition can include hyaluronic acid (paragraph 25) and hydroxypropylmethyl cellulose (HPMC) (paragraph 59). The working examples teach the combination of 0.5% HPMC and 0.5% Scleroglucan (page 11, Example 8, Table 5, ID 21). The addition of a tonicity modifier is also taught (paragraph 59).

Singh et al does not teach the instantly claimed composition as a preferred embodiment. Neither does Singh et al teach the addition of sorbitol as a hexahydric alcohol.

Olejnik et al teaches tonicity adjusting agents known in the art include mannitol and sorbitol.

Olejnik et al does not teach the addition of the gum components.

Gohzu et al teaches trishydroxymethylaminomethane is known to be a buffering agent where at an amount between 5-100 mM, the composition generally achieves a pH of from 6.0 to 7.5 (claim 6).

Olejnlk et al does not teach the addition of the gum components.

It would be obvious to one of ordinary skill in that to substitute the disclosed "gum" compounds, such as hyaluronic acid for Scleroglucan (or in addition to Scleroglucan) in the working example ID 21 where the prior art discloses the ability to substitute the same and the benefit of adjusting the viscosity by doing so. The addition of a tonicity adjusting agent, such as the common tonicity agents of Olejnlk, would be obvious where the primary reference suggests the same. Finally, where the addition of buffering agents is taught, the amount of buffering agent would be a matter of routine optimization based on the desire to achieve a physiological pH similar to that disclosed in Gohzu et al.

With regard to the viscosity, percentage of quenching, and shear-viscosities, these appear to be known properties of a liquid composition, such that their determination would have been obvious to one of ordinary skill in the art using no more than routine experimentation where the primary reference teaches the selection of gums is used to produce a proper viscosity. The quenching appears to be an intended use of the composition and shear-viscosity appears to be a function of the resulting composition.

Where the specific combination of features claimed is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several

variables does not necessarily give rise to anticipation. *Corning Glass Works v. Sumitomo Elec.*, 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S.Ct. 1727, 1740 (2007)(quoting *Sakraida v. A.G. Pro*, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (*Id.*). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." *Id.* at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of gums from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

Claim 20 is rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al (US Pregrant Pub 2003/0232089) in view of Olejnik et al (US 5,597,599) and Gohzu et al (US 5,013,445), further in view of Cantoro et al (US 5,770,628).

Singh et al, Olejnik et al, and Gohzu et al are discussed above.

Cantoro et al teaches the use of hyaluronic acid and its salts in the range of 500 to 4,000 kD for ophthalmic preparations (abstract, claim 1).

Where the additional art teaches the mass of hyaluronic acid and its salts useful in the same type of composition instantly claimed, an ophthalmic preparation, it would be obvious to one of ordinary skill to use hyaluronic acids of the disclosed mass.

Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al (US Pregrant Pub 2003/0232089) in view of Olejnik et al (US 5,597,599) and Gohzu et al (US 5,013,445), further in view of Katz (US 4,287,175).

Singh et al, Olejnik et al, and Gohzu et al are discussed above.

Katz discloses the use of HPMC having a molecular weight of from about 10,000 to 1,000,000 or more, particularly up to about 200,000 and especially about 80,00 to about 125,000 in ophthalmic solutions.

It would be obvious to one of ordinary skill when selecting the HPMC to use HPMC compounds known to be used in ophthalmic solutions, such as disclosed in Katz.

(10) Response to Argument

Appellants responded to the rejection based on five groupings, Group A (claims 1, 6, 8-10, 20, and 25-28), Group B (claim 7), Group C (claim 11), Group E (claim 22) and Group F (claim 47). Examiner notes there does not appear to be a Group D present in the Appeal Brief.

First, Appellants assert with respect to Group A, the term viscoelastic in the preamble requires the composition exhibit a viscosity profile recognized by one of ordinary skill in the art as a viscoelastic composition. Then Appellants assert there is no motivation to choose HPMC from the list of ten acceptable mucoadhesive polymers, or hyaluronic acid as an additional optional mucoadhesive polymer, given the large number of possible combinations. Appellants assert the large number of possibilities alone is sufficient to defeat the Examiner's alleged *prima facie* case of obviousness. Further, Appellants assert Singh directs one of ordinary skill to use a combination of gums to produce unexpected advantages over individual gums, where a nonionic gum is used in combination with an anionic gum.

In response to Group A arguments, Appellants appear to focus on one embodiment taught by the prior art. Specifically, Singh states "anionic gum is preferably combined with a neutral gum since the combination modulates the loss of viscosity of the two individuals." (paragraph 42). But, a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments. Merck & Co. v. Biocraft Laboratories, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989).

Instead, Examiner looks to the broader teaching of Singh et al (claim 1), which teaches a composition suitable for topical administration to the eye, comprising a set of at least two ophthalmically compatible polymers, selected from a claimed Markush grouping (without the specific ionic requirements suggested in the preferred embodiment of paragraph 42). Those combinations include the specific combination of scleroglucan and HPMC as one of the preferred embodiments (see claim 2).

Singh et al teaches:

The term "gum", as used herein, refers to any synthetic polymer, natural polysaccharide, or derivatized natural polysaccharide that is ophthalmically compatible and that increases the viscosity of a solution sufficiently to increase the viscosity of the solution in which it is found or to transform a drop of the solution into a semi-solid or gelatinous state after administration to an eye of a warm-blooded mammal. Examples of synthetic polymer gums include, but are not limited to, polyethylene glycol, polyvinyl pyrrolidone, carboxymethyl cellulose, polyvinyl alcohol and derivatives thereof, and Carbopol and derivatives thereof. Examples of natural polysaccharide gums include, but are not limited to, carrageenan, konjac, sodium alginate, aloe vera gel, agarose, guar, pectin, tragacanth, acacia, Arabic, curdlan, gellan, xanthan, scleroglucan, hyaluronic acid, or chitosan. Examples of derivatized natural polysaccharide gums include, but are not limited to, propyleneglycol alginate and hydroxypropyl guar. (paragraph 25)

While claim 2 further limits claim 1 for some embodiments, when interpreting claim 1, one of ordinary skill would look to the specification, and recognize gums may include natural polysaccharide gums, which include among other gums, scleroglucan and hyaluronic acid (Singh et al paragraph 25). The purpose of the gums specifically disclosed to increase the viscosity to transform a drop of the solution into a semi-solid or gelatinous state after administration to an eye of a warm-blooded mammal (Singh et al specification paragraph 25). Thus, it would be reasonable to pick and choose from

among the various gums in order to find a combination which results in the desired viscosity (i.e. viscoelastic composition) where the selection of a known material based on its suitability for its intended use supported a prima facie obviousness determination in Sinclair & Carroll Co. v. Interchemical Corp., 325 U.S. 327, 65 USPQ 297 (1945)

With regards to the number of potential combinations, here, the components are disclosed as substituted components which modify the viscosity of the resulting composition. Thus, the limited number of related gums would not be outside the reasoning of KSR, given they are reasonably expected to have a predictable result when added, i.e. viscosity is modified.

With respect to Group B, Appellants assert it would not be obvious to modify Singh to an ionic osmolality agent, where the cited prior art prefers non-ionic osmolality agents, and the primary reference uses sodium chloride as an osmolality agent with a phosphate buffer.

In response, Examiner notes the prior art specifically teaches the inclusion of a pH adjusting agent, which may include tris-hydroxymethylaminomethane (Singh et al paragraph 94). Examiner further cited Gohzu et al to teach the amount of buffer commonly required to achieve a desired ophthalmically suitable pH of from 6.0 to 7.5 (Gohzu et al claim 6). Note, Examiner should not be questioned for the application of additional art to further buttress a prima facie case of obviousness.

Examiner previously cited Olejnik et al, which teaches in addition to mannitol, sorbitol may also be used as a tonicity adjusting agent. Again, the substitution of

compounds known to have a common function, i.e. adjusting the tonicity, would be well within the skill of the skilled artisan.

With regards to Group C, Appellants assert the quenching properties of the combination of tris-hydroxymethylaminomethane and sorbitol had the best free-radical quenching properties.

While this appears to be an assertion of possible unexpected result or synergistic properties, such an assertion fails for numerous reasons. First, where a pH balancing agent and tonicity agent are included in a composition, one of ordinary skill would expect a longer shelf life, given the purpose of adjusting the pH and tonicity would be to optimize the properties which would improve not only application, but also stability. Second, the asserted results are not supported by factual evidence. Instead, Appellants point to their specification which vaguely references the components alone have stability improving properties, but the combination has the best stability properties, such is not sufficient to show unexpected results from the combination.

With regards to Group E, Appellants assert there is no guidance in Singh et al to select a specific grade of HPMC.

Examiner notes that the general teaching of Singh et al to use HPMC would lead one of ordinary skill in the art to use HPMC which are known in the art, such as disclosed in Olejnik. Appellants fail to provide evidence suggesting the selection of high molecular weight HPMC would result in a non-viscoelastic composition.

With regards to Group F, Appellants assert claim 42 is nonobvious for the same reasons as claims 1, 26, and 27, given the large number of potential combinations.

Examiner discussed claims 1, 26, and 27 above, and where the reasons are rebutted for those claims, the rejection for claim 42 is likewise rebutted.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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